

REPLACEMENT
ART 34.2

CLAIMS

1. A method for generating an antigen presenting cell (APC) which presents an autoantigen associated with an autoimmune disease, said method comprising collecting a sample of hemopoetic stem cells (HSCs) and/or hemopoetic progenitor cells (HPCs) from a subject, introducing into one or more HSCs and/or HPCs genetic material encoding said autoantigen under conditions wherein said genetic material is expressed so that the HSCs and/or HPCs produce said autoantigens.
2. The method of claim 1, wherein said APC is selected from the group consisting of a dendritic cell, B-lymphocyte, epithelial cell, monocyte and macrophage.
3. The method of claim 2, wherein said APC is a dendritic cell.
4. The method of claim 1, wherein said subject is selected from the group consisting of a human, primate, sheep, horse, cow, donkey, pig, goat, rabbit, mouse, rat, guinea pig, dog, cat, bird, chicken, bantams, geese and turkeys.
5. The method of claim 1, wherein said subject is a human.
6. The method of claim 1, wherein said HSCs and/or HPCs are derived from a source selected from the group consisting of bone marrow from hipbone, bone marrow, cord blood, blood from liver, blood from a tissue and PBMCs.
7. The method of claim 6, wherein said HSCs and HPCs are derived from bone marrow from hipbone.
8. The method of claim 1, wherein said autoantigen is associated with a disease selected from the group consisting of type 1 diabetes or insulin-dependent diabetes, systemic lupus, Crohn's disease, cardiomyopathy, hemolytic anemia, fibromyalgia, Graves' disease, ulcerative colitis, vasculitis, multiple sclerosis, myasthenia gravis,

REPLACED BY
ART 34 AANDT

myositis, neutropenia, psoriasis, chronic fatigue syndrome, juvenile arthritis, juvenile diabetes, scleroderma, psoriatic arthritis, Sjogren's syndrome, rheumatic fever, rheumatoid arthritis, sarcoidosis, idiopathic thrombocytopenic purpura (ITP), Hashimoto's disease, mixed connective tissue disease, interstitial cystitis, pernicious anemia, leukoencephalitis, alopecia areata, ankylosing spondylitis, primary biliary cirrhosis, anti-GBM nephritis, anti-TBM nephritis, anti-phospholipid syndrome, polymyalgia rheumatica, polymyositis, autoimmune Addison's disease, chronic active hepatitis, vitiligo, autoimmune hyperlipidemia, autoimmune myocarditis, temporal arteritis, autoimmune thyroid disease, axonal and neuronal neuropathies, Behçet's disease, bullous pemphigoid, allergic asthma, osteoarthritis, Chagas' disease, uveitis, chronic inflammatory demyelinating polyneuropathy (CIDP), cicatricial pemphigoid/benign mucosal pemphigoid, Cogan's syndrome, congenital heart block, Coxsackie myocarditis, demyelinating neuropathies, dermatomyositis, discoid lupus, phacoantigenic uveitis, polyarteritis nodosa, Dressler's syndrome, essential mixed cryoglobulinemia, Evan's syndrome, Goodpasture's syndrome, allergic rhinitis, Guillain-Barré syndrome, hypogammaglobulinemia, inclusion body myositis, vesiculobullous dermatosis, Wegener's granulomatosis, Ménière's disease, Lambert-Eaton syndrome, Mooren's ulcer, non-typical celiac disease, ocular cicatricial pemphigoid, pemphigus vulgaris, perivenous encephalomyelitis, post-pericardiotomy syndrome, scleritis, sperm and testicular autoimmunity, Stiff man's syndrome, subacute bacterial endocarditis (SBE), sympathetic ophthalmia, transverse myelitis and necrotizing myelopathy, type 1 autoimmune polyglandular syndrome, type 1I autoimmune polyglandular syndrome, pernicious anaemia and endometriosis.

9. The method of claim 1, wherein said autoimmune disease is insulin dependent diabetes.

10. The method of claim 1, wherein said autoantigen is proinsulin or an immunogenic homolog, antigen derivative, part, fragment or portion thereof.

11. The method of claim 10, wherein said proinsulin is of human origin.

REPLACED BY
ART 84 A5DT

12. The method of claim 10, wherein said proinsulin is a humanized proinsulin, wherein said proinsulin is derived from the group selected from cow, pig, sheep, horse, goat, mouse and rat.
- 5 13. A method of preventing or treating an autoimmune disease in a subject comprising introducing into said subject an APC which presents an autoantigen associated with an autoimmune disease, said method comprising collecting a sample of hemopoietic stem cells (HSCs) and/or hemopoietic progenitor cells (HPCs) from a subject, introducing into one or more HSCs and/or HPCs genetic material encoding said autoantigen under conditions
10 wherein said genetic material is expressed so that the HSCs and/or HPCs produce said autoantigens.
14. The method of claim 13, wherein said APC is selected from a dendritic cell, B-lymphocyte, epithelial cell, monocyte and macrophage.
- 15 15. The method of claim 14, wherein said APC is a dendritic cell.
16. The method of claim 13, wherein said subject is selected from the group consisting of a human, primate, sheep, horse, cow, donkey, pig, goat, rabbit, mouse, rat, guinea pig,
20 dog, cat, bird, chicken, bantams, geese and turkeys.
17. The method of claim 13, wherein said subject is a human.
18. The method of claim 13, wherein said cell is derived from bone marrow from the
25 hip bone, bone marrow, cord blood, blood from liver, blood from a tissue and PBMCs.
19. The method of claim 18, wherein said cell is derived from bone marrow from a hip bone.
- 30 20. The method of claim 13, wherein said autoantigen is associated with a disease selected from the group consisting of type 1 diabetes or insulin-dependent diabetes,

REPLACED BY
ART 34 AMDT

systemic lupus, Crohn's disease, cardiomyopathy, hemolytic anemia, fibromyalgia, Graves' disease, ulcerative colitis, vasculitis, multiple sclerosis, myasthenia gravis, myositis, neutropenia, psoriasis, chronic fatigue syndrome, juvenile arthritis, juvenile diabetes, scleroderma, psoriatic arthritis, Sjogren's syndrome, rheumatic fever, rheumatoid arthritis, sarcoidosis, idiopathic thrombocytopenic purpura (ITP), Hashimoto's disease, mixed connective tissue disease, interstitial cystitis, pernicious anemia, leukoencephalitis, alopecia areata, ankylosing spondylitis, primary biliary cirrhosis, anti-GBM nephritis, anti-TBM nephritis, anti-phospholipid syndrome, polymyalgia rheumatica, polymyositis, autoimmune Addison's disease, chronic active hepatitis, vitiligo, autoimmune hyperlipidemia, autoimmune myocarditis, temporal arteritis, autoimmune thyroid disease, axonal and neuronal neuropathies, Behçet's disease, bullous pemphigoid, allergic asthma, osteoarthritis, Chagas' disease, uveitis, chronic inflammatory demyelinating polyneuropathy (CIDP), cicatricial pemphigoid/benign mucosal pemphigoid, Cogan's syndrome, congenital heart block, Cocksackie myocarditis, demyelinating neuropathies, dermatomyositis, discoid lupus, phacoantigenic uveitis, polyarteritis nodosa, Dressler's syndrome, essential mixed cryoglobulinemia, Evan's syndrome, Goodpasture's syndrome, allergic rhinitis, Guillain-Barré syndrome, hypogammaglobulinemia, inclusion body myositis, vesiculobullous dermatosis, Wegener's granulomatosis, Ménière's disease, Lambert-Eaton syndrome, Mooren's ulcer, non-typical celiac disease, ocular cicatricial pemphigoid, pemphigus vulgaris, perivenous encephalomyelitis, post-pericardiotomy syndrome, scleritis, sperm and testicular autoimmunity, Stiff man's syndrome, subacute bacterial endocarditis (SBE), sympathetic ophthalmia, transverse myelitis and necrotizing myelopathy, type 1 autoimmune polyglandular syndrome, type 1I autoimmune polyglandular syndrome, pernicious anaemia and endometriosis.

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21. The method of claim 13, wherein said autoimmune disease is insulin-dependant diabetes.

22. The method of claim 13, wherein said autoantigen is proinsulin or an immunogenic homolog, derivative, part, fragment or portion thereof.

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- 36 -

REPLACED BY
ART 94 AMDT

23. The method of claim 22, wherein said proinsulin is of human origin.
24. The method of claim 22, wherein said proinsulin is a humanised proinsulin,
wherein said proinsulin is derived from the group selected of pig, cow, sheep, horse, goat,
5 mouse and rat.
25. A method for treating or preventing an autoimmune disease in a subject
comprising,
- (a) collecting a sample of hemopoetic stem cells (HSCs) and/or hemopoetic
10 progenitor cells (HPCs) from a subject;
 - (b) introducing into one or more HSCs and/or HPCs genetic material encoding
said autoantigen under conditions wherein said genetic material is expressed so that the
HSCs and/or HPCs produce said autoantigens; and
 - (c) infusing or introducing said genetically modified cells into said subject.
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26. The method of claim 25, wherein said HSCs and/or HPCs undergo cytokine
mediated mobilisation.
27. The method of claim 25, wherein said subject is selected from the group consisting
20 of human, primate, sheep, horse, cow, donkey, pig, goat, rabbit, mouse, rat, guinea pig,
dog, cat, bird, chicken, bantams, geese and turkeys.
28. The method of claim 25, wherein said subject is a human.
- 25 29. The method of claim 25, wherein said HSCs and HPCs are derived from a source
selected from bone marrow from the hipbone, bone marrow, cord blood, blood from liver,
blood from a tissue and PBMCs.
30. The method of claim 29, wherein said HSCs and HPCs are derived from bone
30 marrow from a hipbone.

REPLACED BY
ART 34 ANDT

31. The method of claim 25, wherein said autoantigen is associated with a disease selected from the group consisting of type 1 diabetes or insulin-dependent diabetes, systemic lupus, Crohn's disease, cardiomyopathy, hemolytic anemia, fibromyalgia, Graves' disease, ulcerative colitis, vasculitis, multiple sclerosis, myasthenia gravis, myositis, neutropenia, psoriasis, chronic fatigue syndrome, juvenile arthritis, juvenile diabetes, scleroderma, psoriatic arthritis, Sjogren's syndrome, rheumatic fever, rheumatoid arthritis, sarcoidosis, idiopathic thrombocytopenic purpura (ITP), Hashimoto's disease, mixed connective tissue disease, interstitial cystitis, pernicious anemia, leukoencephalitis, alopecia areata, ankylosing spondylitis, primary biliary cirrhosis, anti-GBM nephritis, anti-TBM nephritis, anti-phospholipid syndrome, polymyalgia rheumatica, polymyositis, autoimmune Addison's disease, chronic active hepatitis, vitiligo, autoimmune hyperlipidemia, autoimmune myocarditis, temporal arteritis, autoimmune thyroid disease, axonal and neuronal neuropathies, Behçet's disease, bullous pemphigoid, allergic asthma, osteoarthritis, Chagas' disease, uveitis, chronic inflammatory demyelinating polyneuropathy (CIDP), cicatricial pemphigoid/benign mucosal pemphigoid, Cogan's syndrome, congenital heart block, Cocksackie myocarditis, demyelinating neuropathies, dermatomyositis, discoid lupus, phacoantigenic uveitis, polyarteritis nodosa, Dressler's syndrome, essential mixed cryoglobulinemia, Evan's syndrome, Goodpasture's syndrome, allergic rhinitis, Guillain-Barré syndrome, hypogammaglobulinemia, inclusion body myositis, vesiculobullous dermatosis, Wegener's granulomatosis, Ménière's disease, Lambert-Eaton syndrome, Mooren's ulcer, non-typical celiac disease, ocular cicatricial pemphigoid, pemphigus vulgaris, perivenous encephalomyelitis, post-pericardiotomy syndrome, scleritis, sperm and testicular autoimmunity, Stiff man's syndrome, subacute bacterial endocarditis (SBE), sympathetic ophthalmia, transverse myelitis and necrotizing myelopathy, type 1 autoimmune polyglandular syndrome, type 1I autoimmune polyglandular syndrome, pernicious anaemia and endometriosis.

32. The method of claim 25, wherein said autoimmune disease is insulin-dependant diabetes.

- 38 -

REPLACED BY
ART 34 AMDT

33. The method of claim 25, wherein said autoantigen is proinsulin or an immunogenic homolog, derivative, part, fragment or portion thereof.

34. The method of claim 33, wherein said proinsulin is of human origin.

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35. The method of claim 34, wherein said proinsulin is a humanized proinsulin, wherein said proinsulin is derived from a source selected from the group consisting of pig, cow, sheep, horse, goat, mouse and rat.

10 36. A kit in multiple compartmental form, said kit comprising a first compartment adapted to receive a source of HSCs and/or HPCs from a subject; a second compartment adapted to contain genetic material encoding an autoantigen; optionally a third or more compartments adapted to contain reagents wherein said kit comprises instructions for use comprising in a method comprising collecting a sample of hemopoetic stem cells (HSCs)
15 and/or hemopoetic progenitor cells (HPCs) from a subject, introducing into one or more HSCs and/or HPCs genetic material encoding said autoantigen under conditions wherein said genetic material is expressed so that the HSCs and/or HPCs produce said autoantigens.

20 37. A subject comprising an introduced APC, wherein said APC is generated using a method comprising the steps of collecting a sample of hemopoetic stem cells (HSCs) and/or hemopoetic progenitor cells (HPCs) from a subject, introducing into one or more HSCs and/or HPCs genetic material encoding said autoantigen under conditions wherein said genetic material is expressed so that the HSCs and/or HPCs produce said
25 autoantigens.

38. The use of an APC which has been genetically modified to present an autoantigen associated with a disease in the manufacture of a medicament for the treatment of an autoimmune disease, wherein said APC is generated from a HSCs and/or HPCs.

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**REPLACED BY
ART 34 AMDT**

39. The use according to claim 38, wherein said APC is selected from the group consisting of a dendritic cell, B-lymphocyte, epithelial cell, monocyte and macrophage.
40. The use according to claim 2, wherein said APC is a dendritic cell.
- 5 41. The use according to claim 38, wherein said HSCs and/or HPCs are derived from a source selected from the group consisting of a human, primate, sheep, horse, cow, donkey, pig, goat, mouse, rat, guinea pig, dog, cat, chicken, bantam hen, geese and turkey.
- 10 42. The use of claim 41, wherein said HSCs and/or HPCs are derived from a human.
43. The use of claim 38, wherein said HSCs and/or HPCs are derived from a source selected from the group consisting of bone marrow from hipbone, bone marrow, cord blood, blood from liver, blood from a tissue and PBMCs.
- 15 44. The use of claim 38, wherein said autoantigen is associated with a disease selected from the group consisting of type 1 diabetes or insulin-dependent diabetes, systemic lupus, Crohn's disease, cardiomyopathy, hemolytic anemia, fibromyalgia, Graves' disease, ulcerative colitis, vasculitis, multiple sclerosis, myasthenia gravis, myositis, neutropenia, psoriasis, chronic fatigue syndrome, juvenile arthritis, juvenile diabetes, scleroderma, psoriatic arthritis, Sjogren's syndrome, rheumatic fever, rheumatoid arthritis, sarcoidosis, idiopathic thrombocytopenic purpura (ITP), Hashimoto's disease, mixed connective tissue disease, interstitial cystitis, pernicious anemia, leukoencephalitis, alopecia areata, ankylosing spondylitis, primary biliary cirrhosis, anti-GBM nephritis, anti-TBM nephritis, 20 anti-phospholipid syndrome, polymyalgia rheumatica, polymyositis, autoimmune Addison's disease, chronic active hepatitis, vitiligo, autoimmune hyperlipidemia, autoimmune myocarditis, temporal arteritis, autoimmune thyroid disease, axonal and neuronal neuropathies, Behçet's disease, bullous pemphigoid, allergic asthma, osteoarthritis, Chagas' disease, uveitis, chronic inflammatory demyelinating 25 polyneuropathy (CIDP), cicatricial pemphigoid/benign mucosal pemphigoid, Cogan's syndrome, congenital heart block, Coxsackie myocarditis, demyelinating neuropathies, 30

**REPLACED BY
ART 34 AMDT**

- 40 -

- dermatomyositis, discoid lupus, phacoantigenic uveitis, polyarteritis nodosa, Dressler's syndrome, essential mixed cryoglobulinemia, Evan's syndrome, Goodpasture's syndrome, allergic rhinitis, Guillain-Barré syndrome, hypogammaglobulinemia, inclusion body myositis, vesiculobullous dermatosis, Wegener's granulomatosis, Ménière's disease,
- 5 Lambert-Eaton syndrome, Mooren's ulcer, non-typical celiac disease, ocular cicatricial pemphigoid, pemphigus vulgaris, perivenous encephalomyelitis, post-pericardiotomy syndrome, scleritis, sperm and testicular autoimmunity, Stiff man's syndrome, subacute bacterial endocarditis (SBE), sympathetic ophthalmia, transverse myelitis and necrotizing myelopathy, type 1 autoimmune polyglandular syndrome, type 1I autoimmune
- 10 polyglandular syndrome, pernicious anaemia and endometriosis.

45. The use of claim 38, wherein said autoimmune disease is insulin-dependant diabetes.

- 15 46. The use of claim 38, wherein said autoantigen is proinsulin or an immunogenic homolg, derivative, part, fragment or portion thereof.

47. The use of claim 46, wherein said proinsulin is of human origin.

- 20 48. The use of claim 38, wherein said proinsulin is a humanized proinsulin, wherein said proinsulin is derived from a source selected from the group consisting of pig, cow, sheep, horse, goat, mouse and rat.